Acetylcholinesterase Inhibitors* (AChEI) to Treat Dementia: 2015 Update

Criteria for Use

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VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

***AChEIs include donepezil, galantamine, and rivastigmine.**

The Product Information should be consulted for detailed prescribing information.

For Additional information on the CFU see the accompanying VA National PBM-MAP-VPE Evidence Summary at the end of this document.

Preliminary Considerations

The VA TEAM-AD study found vitamin E 1000 IU twice a day in combination with an AChEI significantly slowed progression in ADL decline, 19% per year or 6.2 months delay, in Veterans diagnosed with mild to moderate AD. Veterans assigned to memantine with or without vitamin E declined more rapidly, however not as rapidly as those assigned to an AChEI plus placebo. An earlier non-VA trial found vitamin E 1000 IU twice a day significantly increased survival, delayed institutionalization, loss of ADLs, and progression to severe dementia in patients with moderate AD. (See Evidence Summary for more information).

Exclusion Criteria *If ANY items below is checked, then the patient should NOT receive an AChEI.*

☐ Dementia diagnosis other than AD, mixed AD + vascular, Lewy Body Dementia or associated with Parkinson's disease.
☐ Bradycardia (≤50 bpm), syncope
☐ Chronic alcoholism
☐ Chronic diarrhea
☐ Severe hepatic impairment (Child-Pugh >10)
☐ The patient's functional status has declined to the extent that their speech is limited and noncommunicative, ambulation is no longer possible, or their ability to hold their head up independently has been lost, e.g., Functional Assessment Scale (FAST) Stage 7a-f FAST Scale
☐ Frontotemporal dementia (AChEI likely to worsen behavior[1])

Inclusion Criteria
Initial Prescription (all of the following must be met)

☐ A diagnosis of ☐ Alzheimer's disease (AD), ☐ mixed (AD and vascular) dementia, ☐ Lewy Body Dementia, or ☐Dementia associated with Parkinson's disease. (*Check all that apply*)
For patients with a diagnosis of Alzheimer's disease (AD), has the patient been started on vitamin E (alpha tocopherol) 1000 IU twice a day? ☐ Yes ☐ No ☐ Not clinically indicated
Indicate the stage of dementia (*Check only one*)
☐ Mild ☐ Moderate ☐ Severe
Which instrument was used to stage the illness? (*See Monitoring*)
☐ FAST ☐ GDS ☐ CDR ☐ Other
Indicate the reasons an AChEI is being started (*Check all that apply*)

☐ Memory loss or impaired cognition ☐ ADL performance, self-care or cooperation with care ☐ Behavior

☐ For patients who are unable to manage their medications, a caregiver(s) is available to assist with medication administration.
☐ The patient's medication regimen has been reviewed and all unnecessary anticholinergic medications have been discontinued.
☐ No exclusion or discontinuation criteria are met.

Rivastigmine Transdermal (In addition to the above)
☐ The patient could not tolerate oral donepezil or oral galantamine due to gastrointestinal side effects **OR**
☐ The patient cannot take medication by mouth

Initial Renewal Criteria after 3 months on a therapeutic dose; See Dosing (all must be met)[2]

- ☐ The patient is taking a therapeutic dose
- ☐ For patients who are unable to manage their medications, a caregiver(s) is available to assist with medication administration.
- ☐ The patient and/or caregiver and prescriber agree that the patient has benefited from the AChEI and wish to continue, i.e., continuation is still in line with the goals of treatment and treatment targets. This discussion and decision are documented in the patient's medical record. Please check the reason for continuation (*Check all that apply*):
  ☐ Memory loss or impaired cognition ☐ ADL performance, self-care or cooperation with care ☐ Behavior
- ☐ The patient's medication regimen has been reviewed and all unnecessary anticholinergic drugs have been discontinued.
- ☐ No exclusion criteria or discontinuation criteria are met.

Renewal Criteria Every 12 Months (all must be met)

- ☐ The dementia diagnosis has not changed
- ☐ The patient is taking a therapeutic dose
- ☐ For patients who are unable to manage their medications, a caregiver(s) is available to assist with medication administration.
- ☐ The patient and/or caregiver and prescriber agree that the patient has benefited from the AChEI and wish to continue, i.e., continuation is still in line with the goals of treatment and treatment targets. This discussion and decision are documented in the patient's medical record. Please check the reason for continuation:
  ☐ Memory loss or impaired cognition ☐ ADL performance, self-care or cooperation with care ☐ Behavior
- ☐ The patient's medication regimen has been reviewed and all unnecessary anticholinergic drugs have been discontinued.
- ☐ No exclusion or discontinuation criteria are met.

Discontinuation Criteria (if any of the following is checked the AChEI should be discontinued)

- ☐ Poor compliance
- ☐ Persistent side effects, including morbid weight loss
- ☐ Mutual agreement between patient and/or caregiver and prescriber.
- ☐ Permanent loss of caregiver to assist with medication management, if the patient is unable to self-manage medications.
- ☐ The patient's functional status has declined to the extent that their speech is limited and noncommunicative, ambulation is no longer possible, or their ability to hold their head up independently has been lost, e.g., Functional Assessment Scale (FAST) Stage 7a-f FAST Scale
- ☐ Bradycardia ($\leq$50 bpm), syncope
- ☐ Chronic alcoholism
- ☐ Chronic diarrhea
- ☐ Severe hepatic impairment (Child-Pugh $\geq$10)

Monitoring

Monitor for the following and ask patients and their caregivers about signs or symptoms of adverse effects.

- Weight and appetite - weight loss (unintended), dyspepsia, nausea, vomiting, and decreased appetite
- Chronic diarrhea or fecal incontinence
- Heart rate – bradycardia, heart block and syncope are associated with AChEIs

The Functional Assessment Staging (FAST) scale is one of three instruments for staging dementia available in CPRS Mental Health Assistant; the other two are the Global Deterioration Scale and the Clinical Dementia Rating scale.

Staging of Dementia[3]

Stage of Impairment	Corresponding Scale	Description
Mild	MMSE >18 GDS or FAST stage 4 CDR = 1	Difficulty balancing a checkbook, preparing a complex meal, or managing a difficult medication schedule.
Moderate	MMSE = 10 – 18 GDS or FAST stages 5 & 6 CDR = 2	Above plus difficulties with simpler food preparation, household cleanup, and yard work; may require some assistance with some self-care
Severe	MMSE <10 GDS or FAST stages 6 & 7 CDR = 3	Require considerable or total assistance with ADLs such as dressing, bathing and toileting
Terminal	Often unable to complete GDS or FAST stage 7	Noncommunicative, nonambulatory or bed bound, require constant care, develop contractures, susceptible to infections, pressure sores and accidents.

MMSE = Mini Mental Status Exam; GDS = Global Deterioration Scale; FAST = Functional Assessment Staging; CDR= Clinical Dementia Rating; ADLs = Activities of Daily Living

Issues for Consideration

Combination of an AChEI and Memantine[4-9]

The combination of an AChEI and memantine is permissible for Veterans meeting the criteria for use for both drugs. The evidence, and its interpretation, of adding memantine to an AChEI is mixed. While individual Veterans may benefit from a trial of combination therapy, unless clear benefit is documented, ongoing combination therapy should not routinely be continued. (See AChEI and Memantine CFU: Evidence Summary) The combination of an AChEI, memantine and Vitamin E has not been studied in moderate-severe AD.

Acetylcholinesterase Inhibitor Dosing

Drug	Initial Dose	Titration Schedule Every	Recommended Dose	Minimum Therapeutic Dose	Formulations
Donepezil	5 mg daily	4 weeks	10 mg daily	5 mg daily	5, 10 and *23 mg
Galantamine IR	4 mg twice a day	4 weeks	12 mg twice a day	8 mg twice day	4, 8, 12 mg
Galantamine ER	8 mg daily	4 weeks	24 mg daily	16 mg daily	8, 12, 24 mg
*Rivastigmine	1.5 mg twice a day	4 weeks	6 mg twice a day	3 mg twice a day	1.5, 3, 4.5, 6 mg
Rivastigmine patch	4.6 mg daily	4 weeks	9.5 mg/day	9.5 mg/day	4.6, 9.5, 13.3 mg

*Non-formulary

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Preliminary Considerations

This section is not a part of the criteria for use and is not intended to influence the approval decision for an AChEI or memantine. The section serves as a reminder to the prescriber to consider the addition of Vitamin E 1,000 IU twice a day, the patient's stage of illness and intended benefit of either an AChEI or memantine.

Vitamin E (as alpha-tocopherol) 1,000 IU twice a day as a treatment for Alzheimer's disease (AD) has been investigated in two clinical trials. The first trial randomized patients with AD of moderate severity to vitamin E + placebo, selegiline 5 mg twice a day + placebo, the combination, or double placebo for two years.[1] The primary outcome was to death, institutionalization, loss of ability to perform 2 of 3 basic ADLs, or severe dementia. After adjustment for baseline MMSE*, all three treatments significantly delayed the primary outcome compared to placebo. The estimated increase in survival over placebo with vitamin E, selegiline, or the combination was 230 days, 215 days, and 145 days, respectively. Falls and syncope were the most common adverse events in all four groups. The overall mortality rate was 10.3%; there were not differences between the groups.

The second trial was conducted by the VA Cooperative Studies Program (TEAM-AD study)[2]. A total of 613 Veterans with mild-moderate dementia were randomized to vitamin 1,000 IU twice a day + placebo, memantine 10 mg twice a day, the combination, or double placebo. All subjects were taking an AChEI prior to enrollment and continued throughout the trial. Patients taking warfarin were excluded. The primary outcome variable was the 78 point ADCS-ADL*. The mean time of follow-up was 2.27 years. Compared to placebo, a significantly slower decline from baseline was found for vitamin E-alone, 3.15 Units (95% CI 0.92-5.39), adjusted p=.03) which corresponds to a 19% per year and a 6.2 months delay in progression. Subjects assigned to the other two treatment arms also demonstrated a non-significant slower decline than the placebo-only group; memantine 1.99 Units, vitamin E + memantine 1.75 Units. Time spent delivering care by the caregiver increased the least in vitamin E arm, but the only significant difference was between vitamin and memantine. None of the changes in the other secondary outcomes (MMSE, ADAS-cog*, and NPI*) were significant. Adverse events and serious adverse events were distributed evenly across all four groups. An infection or infestation, and falls were the most common serious adverse events, ranging from 7-20% and 8%-10%, respectively. Five percent of subjects in each treatment arm experienced bleeding. It is not known why subjects assigned to vitamin E and memantine had the least improvement of the active treatment arms. There are no data on the combination of an AChEI, vitamin E and memantine.

A 2005 meta-analysis[3] associated vitamin E $\geq$400 IU per day with an increased risk of all-cause mortality. The TEAM-AD trial reported annual mortality rates of 7.3% with vitamin E, 11.3% with memantine, 9.0% with the combination, and 9.4% with placebo.

Exclusion Criteria

Bradycardia: The AChEI can increase cholinergic stimulation of the vagus nerve resulting in bradycardia, heart block and syncope. A population-based cohort study found that patients taking an AChEI to experience syncope more frequently than those not taking an AChEI (Hazard Ratio: 1.76; 95% CI 1.57-1.98). Patients taking an AChEI also experienced more syncope-related events: hospitalization (1.69; 1.32-2.15), permanent pacemaker placement (1.49; 1.12-2.00) and hip fracture (1.18; 1.04-1.34).[4]

Chronic Alcoholism/Severe liver disease: Donepezil's clearance is reduced by 20% in patients with stable alcoholic cirrhosis.[5] The dose of galantamine should not exceed 16 mg/day in patients with moderate liver impairment (Child-Pugh score 7-9). Galantamine is not recommended for patients with severe hepatic impairment (C-P score 10-15).[6] Lower doses of rivastigmine are recommended in persons with mild to moderate hepatic impairment (C-P 5-9). There is no data available on the use of the use of rivastigmine in persons with serve hepatic impairment.[7]

Frontotemporal dementia: The available evidence suggests that the AChEI may worsen behavior, particularly disinhibited and compulsive acts.[8]

Inclusion Criteria

Initial Renewal of AChEI after 12 weeks

The efficacy of AChEIs is moderate and coupled with their adverse effect profile, patients, caregivers and clinicians should have a discussion of the drugs' potential benefits and harms. The American Geriatrics Society in collaboration with American Board of Internal Medicine Foundation's "Choosing Wisely" campaign recommends that AChEIs not be prescribed without periodic assessment for perceived cognitive benefits and adverse gastrointestinal effects.[9] In clinical trials of AChEIs, the peak improvement in cognitive measures occurred by week 12.[10-14]

Monitoring

Patients should be monitored for loss of appetite, weight loss, chronic diarrhea, bradycardia, heart block and syncope over the course of treatment with an AChEI. These side effects are justification to discontinue the AChEI. Additional monitoring to stage the progression of the illness using one of the three instruments available in the CPRS Mental Health Assistant (Functional Assessment Staging (FAST) scale, the Global Deterioration Scale or Clinical Dementia Rating Scale is necessary to determine whether there is benefit from drug therapy.

Issues for Consideration

Combination of an AChEI plus Memantine

Five randomized clinical trials and one observational study have evaluated whether the addition of memantine to an AChEI is beneficial compared to continuing the AChEI as monotherapy in patients with Alzheimer's disease (AD). [2, 15-17,19-20] The first trial was 24 weeks in length and employed a randomized, double-blind, placebo-controlled, parallel-group, fixed dose design.[15] Patients (n=404) with moderate to severe AD (Mini Mental Status Exam [MMSE] 5-14) who had been taking donepezil 5 mg or 10 mg daily for more than 6 months and a stable dose for ≥3 months were eligible. Patients continued donepezil

and were assigned to add placebo or memantine 20 mg daily. Results of the primary (ADAS-cog and CIBIC+) and secondary outcome measures are shown in Table 1. Predetermined measures of clinically meaningful differences were not established. All mean differences from baseline between groups favored the addition of memantine. However, the absolute magnitude of the differences was relatively small. For example, the absolute difference between the mean SIB scores was 3.4 points on a 100 point scale. Both groups declined in their ADLs over the course of the study.

Table 1 Results Tariot et al. 2004[15]

Outcome	Treatment	Baseline	Least Square Mean Difference at Wk 24	Absolute Difference Between Groups at Wk 24
SIB 0-100	Placebo Memantine	80 78	-2.5 0.9	3.4
ADCS-ADL 0-54	Placebo Memantine	35.8 35.5	-3.4 -2.0	1.4
*CIBIC+	Placebo Memantine	- -	4.66 4.41	0.25
NPI 0-144	Placebo Memantine	13.4 13.4	3.7 -0.1	3.8
BGP Care Dependency	Placebo Memantine	9.8 9.8	2.3 0.8	1.5

*categorical variable, value shown is at 24 weeks or endpoint
Outcome measures are described on page 10.

The second trial randomized 433 patients and used the same design as the first trial with two differences.[16] First, participants had mild-moderate AD (MMSE 10-22) and second, they could be taking any of the three AChEI marketed provided the dose was therapeutic, treatment was for $\geq$6 months, and the dose had been stable for $\geq$3 months. The ADAS-cog and CIBIC+ were the study's primary outcome measures. The difference in all measures was not significant (Table 2). The authors concluded the addition of memantine did not result in significant benefit.

Table 2 Results Porsteinsson et al. 2008[16]

Outcome	Treatment	Baseline	Score at 24-Wk	Least Square Difference (95% CI)
ADAS-cog 0-70	Placebo Memantine	26.8 27.9	28.0 28.5	-0.7 (-1.8 – 0.4)
*CIBIC+	Placebo Memantine	- -	4.42 4.38	0.0 (-0.2 – 0.2)
ADCS-ADL 0-54	Placebo Memantine	54.8 54.7	52.0 51.8	-0.2 (-1.6 – 1.3)
NPI 0-144	Placebo Memantine	12.3 11.8	12.6 12.9	0.3 (-1.7 – 2.4)
MMSE 0-30	Placebo Memantine	17.0 16.7	16.4 16.5	0.5 (-0.1 – 1.1)

*categorical variable, value shown is at 24 weeks or endpoint
Outcome measures are described on page 10.

The third trial was in 295 persons with moderate-severe AD (MMSE 5-13) and of 52 weeks duration.[17] All participants had been prescribed donepezil for ≥3 months and taking a dose of 10 mg per day for ≥6 weeks. Participants were randomized to one of the following 4 treatment assignments:

- Continue donepezil + memantine 20 mg per day
- Continue donepezil + placebo-memantine
- Placebo (taper and discontinue donepezil) + memantine 20 mg per day
- Placebo (taper and discontinue donepezil) + placebo-memantine

Three comparisons were made in the analysis:

- Continue donepezil + placebo/memantine vs. placebo donepezil + placebo/memantine
- Memantine + placebo/donepezil vs. placebo memantine + placebo/donepezil
- Donepezil + memantine vs. donepezil + placebo

Minimally important clinical differences (MICD) were determined for 3 outcome measures prior to the final analysis based on 0.4 standard deviations of the change from baseline of the first 127 subjects completing the study. Results from the trial are shown in Table 3. Statistically significant changes from baseline were found in MMSE and BADLs when patients continued donepezil versus discontinuing donepezil ($p<.001$ for both) and those who received memantine versus memantine placebo (MMSE $p<.001$, BADLs $p=.02$). The addition of memantine did not result in any change that met the MICD. The authors concluded continuing donepezil in patients with moderate-severe AD provided modest cognitive and functional benefits although the difference in BADLs did not reach the MICD. The discontinuation of donepezil resulted in a loss of benefit (or appearance of withdrawal) that was greater than the MICD for the MMSE, but not any other outcome measures. Even the clinical significance of this difference has been questioned if the MICD is viewed as unity in the confidence interval and its inclusion in the confidence interval signifies lack of significance (as does the inclusion of 1 when interpreting an odds ratio).[17]

Table 3 Results Howard et al. 2013[17]

Comparison	**Overall difference between groups (CI)**		
	MMSE (0-30)	**BADLs (0-60)**	**NPI (0-144)**
Baseline (mean)	9.1	27.7	22.2
Continue D vs. DC	+1.9 (1.3, 2.5)	-3.0 (-4.3, -1.8)	-2.3 (-5.7, 1.1)
Active M vs. Pm	+1.2 (0.6, 1.8)	-1.5 (-2.8,-0.3)	-4.0 (-7.4, -0.6)
Combo vs. D alone	+0.8 (-0.1, 1.6)	-0.5 (-2.2, 1.2)	-5.1 (-9.8,-0.3)
MICD	1.4	3.5	8

The fourth study (MEM-MD-50) compared the addition of memantine 28 mg extended-release or placebo to an AChEI in noninstitutionalized patients with moderate to severe AD (MMSE 3-14, FAST 6a-6b).[19] The 24-week long study used a multinational, randomized, double-blind, placebo-controlled, parallel-group design. The SIB and CIBIC-Plus were the two primary outcome measures using a last observation carried forward approach. A total of 677 subjects were randomized (1:1) with ~80% in each group completing the trial. Small, but statistically significant differences favoring memantine XR were reported for the SIB and CIBIC-Plus as well as secondary outcomes NPI and verbal fluency (Table 4). Predetermined measures of clinically meaningful differences were not established.

Table 4 Results Grossberg et al. 2013[19]

Outcome	Treatment	Baseline	Mean difference from baseline at endpoint (SD)	Least Square Mean Difference Between Groups (95% CI)	p-value
SIB 0-100	Placebo Memantine	75.2 76.8	0.3 (11.5) 2.7 (11.2)	2.6 (1.0, 4.2)	.001
*CIBIC+	Placebo Memantine	4.5 4.5	4.1 (1.2) 3.8 (1.2)	N/A	.008
ADCS-ADL 0-54	Placebo Memantine	32.8 33.1	-1.3 (7.7) -0.7 (6.9)	0.7 (-0.3, 1.8)	.177
NPI 0-144	Placebo Memantine	16.5 17.2	-1.6 (12.7) -4.3 (14.6)	-2.7 (-4.5, -0.8)	.005
Verbal Fluency Test	Placebo Memantine	5.8 5.7	-0.3 (2.5) 0.3 (2.8)	0.5 (0.2, 0.9)	.004

*categorical variable, value shown is at 24 weeks or endpoint
Outcome measures are described on page 10.

The fifth trial was the VA's TEAM-AD trials (see above).[2]

An observational trial to determine if treatment of patients with probable AD (mean MMSE ~18) affected the time to nursing home admission or death followed 934 patients for a mean of 62.3 months.[20] A total of 140 patients were taking an AChEI plus memantine, 387 an AChEI-alone, and 416 neither. Compared to patients not receiving treatment with an ACHEI +/- memantine, nursing home admission was significantly less likely for those taking only an AChEI (HR 0.37, 95% CI 0.2-0.49) and those on the combination (0.29, 0.11-0.76). A comparison of patients taking an AChEI-alone to those on the combination favored the combination (0.31, 0.12-0.8). The time to death was not altered by either treatment.

Memantine for Parkinson's Disease Dementia (PDD) or Lewy Body Dementia (LBD)

Two clinical trials have evaluated memantine as monotherapy for PDD and LBD.[21-23] Both used a 24-week, randomized, double-blind, placebo-controlled design. The first trial randomized 72 patients to placebo (23 PDD, 15 LBD) or memantine 20 mg per day (17 PPD, 17 LBD).[21] The primary outcome measure was the CGIC score (Table 5).

Table 5 Results Aarsland et al. 2009[21]

Treatment Group	Mean (SD) CGIC score at 24 weeks	Mean difference in CGIC score between groups (95% CI)
Memantine	3.5 (1.5)	0.7 (0.004-1.39)
Placebo	4.2 (1.5)	

No difference in MMSE, NPI, DAD or modified UPDRS (secondary outcomes) was found between the two treatments. Scores on a quick test of cognitive speed (AQT) requiring the naming of form stimuli were statistically improved in memantine treated patients. Preliminary descriptive sub-analyses suggest that patients with PDD may have had a greater global response to memantine (mean CGIC scores: memantine 2.9, placebo 4.3).

A 30-week open-label extension trial found 58% of patients reporting loss of benefit after stopping memantine during the washout period compared to 25% who stopped placebo.[22] CGIC scores in both group declined rapidly in both groups, memantine by 1.4 and placebo 0.8 points. Loss of benefit manifested as recurrence of symptoms which resolved with re-initiation of memantine.
The second trial randomized patients with mild-moderate LBD (n=34) and PDD (n=62) to memantine 20 mg/day or placebo.[23] After 24 weeks there were no significant differences in between group differences in the mean change from baseline for any of the outcome measures (ADCS-CGIC, NPI, ADCS-ADL_{23}, UPDRS3 or Zarit scale total). Subgroup analysis found only patients with DLB receiving memantine had significant differences (improvement) in the mean change on the ADCS-CGIC (-0.6, -1.2 to -0.1) and NPI (-5.9, -11.6 to -0.2).

Outcome Measures Used in Clinical Trials

Severe Impairment Battery (SIB) – a 40-item cognitive function assessment instrument for persons with more advanced dementia. The SIB consists of 9 subscales: Social Interaction, Orientation, Visuospatial Ability, Constructional Ability, Language, Memory, Attention, Orienting to Name, and Praxis. Maximum score is 100 (least impaired) minimum score is 0 (most impaired).
Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog) – uses nine items to assess cognitive function in persons with Alzheimer's disease. Scores range from 0 – 70 with lower scores indicating less impairment
Clinician's Interview-Based Impression of Change Plus Caregiver Input scale (CIBIC+) – an independent clinician interviews the patient and caregiver prior to scoring the overall change and change in several domains of patient function using the patient's baseline score as a reference point. The 7-point scale ranges from 1= marked improvement to 4 = no change to 7 = marked worsening.
Alzheimer's Disease Cooperative Study-Activities of Daily Living (ADCS-ADL) scale – a 19 or 23 item measure with a score of 54 or 78 indicating least impaired and 0 indicating most impaired.
Mini Mental Status Exam (MMSE) – a 30-item assessment of cognitive function; a score of 30 is least impaired and 0 is most impaired.
NeuroPsychiatric Inventory (NPI) – assesses frequency and severity of behavioral symptoms based on caregiver interview. Scores range from 0 – 100; higher scores signify greater symptoms.
Behavioral Rating Scale for Geriatric Patients (BGP Care Dependency) - accesses need for care; 0, 1 or 2 (worse).
Bristol Activities of Daily Living (BADLS) – Assesses activities of daily living; scores range from 0 – 60 with higher scores signifying greater impairment.
Disability Assessment for Dementia (DAD) – Measures activities of daily; scores range from 0 - 52 with higher scores signifying better function.
Unified Parkinson's Disease Rating Scale (UPDRS) – Modified scale used to measure motor function; scores range from 0-12 with higher scores meaning more severe parkinsonism.
Zarit scale – Assesses physical, psychological, and social consequences of caregiver burden. Scores range from 0 (best) to 4 (worst).

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